

### **Amendments to the Claims**

This Listing of Claims will replace all prior versions, as Listings, of claims in this application.

### **Listing of Claims:**

1. (currently amended) An isolated polynucleotide encoding a variant cytochrome P450 3A4 (CYP3A4) monooxygenase polypeptide or fragment thereof wherein the polynucleotide is selected from the group consisting of:
  - (a) a polynucleotide ~~having comprising the nucleic acid~~nucleotide sequence of SEQ ID NO: ~~54, 55, 58, 59, 62, 63, 66, 67, 70, 71, 74, 75, 78, 79, 82, 83, 86, 87, 90, 91, 94, 95, 98, 99, 102, 103, 106, 107, 110, 111, 118, 119, 122, 123, 126, 127, 128, 134, 138, 144, 146, 148, 150, 151, 152, 153, 154, 156, 157, 159, 161, 162, 163 or 164;~~
  - (b) a polynucleotide encoding a polypeptide having the amino acid sequence ~~of any one of~~ SEQ ID NO: ~~129, 135, 139, 145, 147, 149, 155, 158 or 160;~~
  - ~~(c) a polynucleotide encoding a CYP3A4 or CYP3A7 polypeptide, wherein said polynucleotide is having at a position corresponding to any one of position 6004, 13908, 14292, 14304, 14323, 14329, 14357, 15753, 20230, 21867, 21868, 21896, 22026, 22041, 23081, 23172, 25925 or 25958 of the CYP3A4 gene (Accession No: AF280107, whereby the nucleotide A of the first ATG encoding the CYP3A4 protein has been taken as position 1) or at a position corresponding to position 1229 of the CYP3A7 (Accession No: gi4503232) a nucleotide exchange, a nucleotide deletion, an additional nucleotide or an additional nucleotide and a nucleotide exchange, wherein said nucleotide deletion at a position corresponding to position 23172 is not resulting in an M to T amino acid substitutuion or is not a T to C nucleotide exchange;~~
  - ~~(d)~~ (dc) a polynucleotide encoding an CYP3A4 ~~or CYP3A7~~ polypeptide, wherein said polynucleotide is having at a position corresponding to any one of position 6004, 13908, 14292, 20230 ~~or 21868~~ of the CYP3A4 gene (Accession No: AF280107, whereby the nucleotide A of the first ATG encoding the CYP3A4 protein has

~~been taken as position 1) an A, at a position corresponding to any one of position 14323, 14329, 21867, 21896, 22026, 22041, 23081 or 25925 of the CYP3A4 gene (Accession No: AF280107, whereby the nucleotide A of the first ATG encoding the CYP3A4 protein has been taken as position 1) a T, at a position corresponding to any one of position 14357, 15753 or 25958 of the CYP3A4 gene (Accession No: AF280107, whereby the nucleotide A of the first ATG encoding the CYP3A4 protein has been taken as position 1) a G, at a position corresponding to any one of position 14304 of the CYP3A4 gene (Accession No: AF280107, whereby the nucleotide A of the first ATG encoding the CYP3A4 protein has been taken as position 1) a C or at a position corresponding to position 1229 of the CYP3A7 gene (Accession No: gi4503232) a G;~~

- (ed) a polynucleotide encoding an CYP3A4 polypeptide, wherein said polypeptide comprises an amino acid substitution at ~~any one of position 56, 130, 170, 174, 363, 373, 416 or 445 of the CYP3A4 polypeptide (Accession No: AF280107); wherein said substitution at a position corresponding to position 445 is not M to T; and~~
- (fe) a polynucleotide encoding an CYP3A4 ~~or CYP3A7~~ polypeptide, wherein said polypeptide comprises an amino acid substitution of ~~G to D at position 56, R to Q at position 130, V to I at position 170, D to H at position 174, T to M at position 363, L to F at position 373 or P to L at position 416 of the CYP3A4 polypeptide (Accession No: AF280107) or T to R at position 409 of the CYP3A7 polypeptide (Accession No: gi4503232).~~

- 2. (cancelled).
- 3. (currently amended) The polynucleotide of claim 1 ~~or 2~~, wherein the nucleotide deletion, addition and/or substitution result in altered expression of the variant CYP3A4 ~~or CYP3A7~~ gene compared to the corresponding wild type gene.

4. (currently amended) A vector comprising the polynucleotide of ~~any one of claim~~[[s]] 1 ~~to~~or 3.
5. (previously presented) The vector of claim 4, wherein the polynucleotide is operatively linked to expression control sequences allowing expression in prokaryotic or eukaryotic cells.
6. (currently amended) An isolated host cell genetically engineered with the polynucleotide of ~~any one of claim~~[[s]] 1 ~~to~~or 3 or the vector of claim 4 or 5.
7. (currently amended) A method for producing a molecular variant CYP3A4 ~~or CYP3A7~~ protein or fragment thereof comprising
  - (a) culturing the host cell of claim 6; and
  - (b) recovering said protein or fragment from the culture.
8. (currently amended) A method for producing cells capable of expressing a molecular variant CYP3A4 ~~or CYP3A7~~ gene comprising genetically engineering cells with the polynucleotide of ~~any one of claim~~[[s]] 1 ~~to~~or 3 or the vector of claim 4 or 5.
- 9-11. (cancelled).
12. (currently amended) An isolated nucleic acid molecule complementary to a polynucleotide of ~~any one of claim~~[[s]] 1 ~~to~~or 3.
13. (previously presented) A vector comprising the nucleic acid molecule of claim 12.
- 14-36. (cancelled).

37. (currently amended) A primer or probe consisting of an oligonucleotide ~~as defined in claim 36~~ of about 15 to 50 nucleotides in length and comprising the nucleotide sequence of SEQ ID NO:90 or a complementary sequence.
38. (cancelled).
39. (currently amended) A composition comprising the polynucleotide of ~~any one of claim[[s]] 1 to or 3, the vector of claim 4 or 5, the host cell of claim 6 or obtained by the method of claim 8, the protein of claim 9, the antibody of claim 10 or 11, the nucleic acid molecule of claim 12, the vector of claim 13, the inhibitor of claim 32 or the primer or probe of claim 37.~~
40. (previously presented) The composition of claim 39 which is a diagnostic or a pharmaceutical composition.